

What is claimed is:

1. A microarray apparatus with enhanced feature detectability comprising:
a control probe comprising a control sequence of nucleic acids attached at one end in an array pattern of features on a surface of a microarray substrate;
an oligomer test probe comprising a sequence of nucleic acids attached at each feature location, such that each feature comprises the control probe and the oligomer test probe; and
a control label associated with the control probe that emits a control signal when exposed to light that is unique to the control probe.
2. The apparatus of Claim 1, wherein the oligomer test probe is attached to an opposite end of the control probe at each feature location and the control probe is a control stilt extending between the oligomer test probe and the surface of the substrate.
3. The apparatus of Claim 1, wherein the oligomer test probe is attached at the surface of the microarray substrate.
4. The apparatus of Claim 1, wherein the oligomer test probe is associated with a test label, wherein the test label emits a test signal when exposed to light, the test signal being different from the control signal.
5. The apparatus of Claim 4, wherein the test label is attached to a test target sample and the oligomer test probe is associated indirectly with the test label by hybridization of the test target to the oligomer test probe upon exposure of the apparatus to the labeled test target sample.
6. The apparatus of Claim 4, wherein the detectability of each feature on the microarray substrate is enhanced upon interrogation with a microarray scanner by detecting the control signal at each feature regardless of the quality of the test label signal at each feature.

7. The apparatus of Claim 1, wherein each feature on the substrate is detected by detecting the control signal upon interrogation with the scanner for a non-destructive quality control evaluation of the apparatus.

8. The apparatus of Claim 1, wherein the control probe is associated directly with the control label.

9. The apparatus of Claim 8, wherein each feature on the substrate is detected by detecting the control signal upon interrogation with a microarray scanner for a non-destructive quality control evaluation of the apparatus.

10. The apparatus of Claim 1, wherein the control label is attached to a control-specific target material that is complementary to the control probe and the control probe is associated indirectly with the control label by hybridization upon exposure of the apparatus to the labeled control target material.

11. The apparatus of Claim 10, wherein the labeled control target is included in a hybridization solution comprising the labeled test target that is complementary to the oligomer test probe, such that upon exposure of the apparatus to the hybridization solution and then a microarray scanner, the control signal from the hybridized control probe provides reference data that can be normalized with test signal data from the hybridized oligomer test probes.

12. The apparatus of Claim 1, wherein the control label comprises a control probe label and a control target label, the control probe label is associated directly with the control probe, the control target label is associated directly with a control-specific target material that is complementary to the control probe, and wherein the control probe label emits a control probe signal and the control target label emits a control target signal that is different from the control probe signal.

13. The apparatus of Claim 12, wherein the labeled control probe is associated indirectly with the control target label by hybridization upon exposure of the apparatus to the labeled control target material, and wherein the control probe signal

is detected in a control probe detection channel and the control target signal is detected in a separate control target detection channel of a microarray scanner upon interrogation of the hybridized apparatus with the scanner.

14. The apparatus of Claim 12, wherein each feature on the microarray is detectable upon interrogation with a microarray scanner for a non-destructive quality control evaluation by detecting the control probe signal before hybridization, and for locating hybridized oligomer test probes on each feature by detecting the control target signal after hybridization.

15. The apparatus of Claim 14, wherein the labeled control target is included in a hybridization solution comprising a labeled test target that is complementary to the oligomer test probe, and wherein the control target signal from the hybridized control probe provides reference data that can be normalized with hybridization data from the hybridized oligomer test probes.

16. A microarray apparatus with enhanced feature detectability having an oligomer test probe attached in an array pattern of features on a substrate, the apparatus comprising:
a control sequence of nucleic acids attached at one end to a surface of the substrate at each feature location; and
a control label associated with the control sequence that emits a control signal when excited by a light.

17. The microarray of Claim 16, wherein the oligomer test probe is attached to an opposite end of the control sequence at each feature location, such that each feature comprises the control probe and the oligomer test probe.

18. The microarray of Claim 16, wherein the oligomer test probe is attached to the surface of the substrate at each feature location, such that each feature comprises the control probe and the oligomer test probe.

19. The microarray of Claim 16, wherein the control label is associated directly with the control sequence, such that upon interrogation with the microarray scanner the control signal is emitted from each feature.

20. The microarray of Claim 16, wherein a test label is attached to a test target sample, the test label emitting a test signal when excited by the light, the test signal being different from the control signal and separately detectable upon interrogation with a microarray scanner, and wherein the test label is associated indirectly with the oligomer test probe upon hybridization of the labeled test target to the oligomer test probe, such that upon interrogation with the microarray scanner, the control sequence emits the control signal at each feature and the test signal is emitted from only those features having a hybridized test probe.

21. The microarray of Claim 20, wherein the control label comprises a control sequence label and a control target label, the control sequence label is associated directly with the control sequence, the control target label is attached to a control target material that is complementary to the control sequence, the control target label is associated indirectly with the labeled control sequence upon hybridization of the labeled control target to the labeled control sequence.

22. The microarray of Claim 20, wherein the control label is attached to a control target material that is complementary to the control sequence, and wherein the control label and the test label are associated indirectly with the control sequence and the oligomer test probe, respectively, upon hybridization of the labeled control target to the control sequence and the labeled test target to the oligomer test probe, such that upon interrogation with the microarray scanner, the hybridized control sequence emits the control signal at each feature.

23. A method of performing a non-destructive quality control evaluation on an array of features on a surface of a microarray substrate comprising the steps of:
providing a labeled control probe to each feature on the surface of the microarray substrate, the labeled control probe emitting a control signal when excited by a light;

interrogating the populated microarray substrate; and
evaluating data acquired from the interrogation before further use of the
populated microarray substrate.

24. The method of performing of Claim 23, wherein the step of interrogating
5 comprises the steps of:

scanning the microarray substrate with a light to excite each labeled control
probe; and

detecting the control signal from the labeled control probe on each feature.

25. The method of performing of Claim 23, wherein the step of evaluating
10 comprises the step of:

using the data acquired for modifying subsequent depositions.

26. The method of performing of Claim 25, further comprising the step of:
subsequently providing an oligomer test probe to each feature of the
microarray substrate based on the acquired data, such that each feature comprises the
15 labeled control probe and the oligomer test probe.

27. The method of performing of Claim 26, wherein the step of evaluating
comprises the step of:

forwarding the data acquired to a user to assist the user in evaluation of
hybridization test results.

28. The method of performing of Claim 23, wherein after the step of
20 evaluating, further comprises the step of:

forwarding the data acquired to a user to assist the user in evaluation of
hybridization test results.

29. The method of performing of Claim 23, further comprising the step of:
25 providing an oligomer test probe to each feature of the microarray substrate,
such that each feature comprises the labeled control probe and the oligomer test
probe, either before or after the step of interrogating.

30. A method of making a microarray with enhanced feature detectability, the microarray having a microarray substrate, the method comprising the steps of:

providing a control probe in an array pattern of features on a surface of the substrate, the control probe being associated with a control label that emits a control signal when excited by a light; and

providing an oligomer test probe to each feature location, such that each feature comprises the control probe and the oligomer test probe.

31. The method of making of Claim 30, wherein the step of providing the control probe comprises the steps of:

10 adding one end of the control probe to the surface within each feature; and

 directly labeling the control probe with the control label.

32. The method of making of Claim 30, wherein the step of providing the control probe comprises the steps of:

adding one end of the control probe to the surface within each feature; and

indirectly associating the control label to the control probe by hybridization

when exposed to a control-specific target material that comprises the control label.

33. The method of making of Claim 30, wherein the step of providing the control probe comprises the steps of:

adding one end of the control probe to the surface within each feature, and

20 directly labeling the control probe with a control probe label of the control label, the control probe label emitting a control probe signal of the control signal; and

indirectly associating a control target label of the control label to the labeled control probe by hybridization when exposed to a control-specific target material that comprises the control target label, the control target label emitting a control target

25 signal of the control signal that is different from the control probe signal.

34. The method of making of Claim 30, wherein the steps of providing the control probe and providing the oligomer test probe comprises the steps of:
adding one end of the control probe to the surface of substrate at each feature location;

[illegible]

adding the oligomer test probe to each feature; and
indirectly associating the control label to the control probe and a test label to the oligomer test probe by hybridization when exposed to a hybridization mixture comprising a labeled test target sample complementary to the oligomer test probe and a labeled control-specific target material complementary to the control probe, wherein the labeled control target material comprises the control label and the labeled test target sample comprises the test label.

35. The method of making of Claim 30, wherein the step of providing the oligomer test probe comprises the steps of:

adding the oligomer test probe to each feature of the substrate; and
directly labeling the oligomer test probe with a test label.

36. The method of making of Claim 30, wherein the step of providing the oligomer test probe comprises the steps of:

adding an oligomer test probe to each feature of the substrate; and
indirectly associating a test label with the oligomer test probe by hybridization
when exposed to a test target material that comprises the test label.

37. The method of making of ~~Claim 30~~, wherein the step of providing the control probe comprises the step of adding one end of the control probe to the surface of the microarray substrate; and the step of providing the oligomer test probes comprises the step of adding the oligomer test probe to an opposite end of the control probe, such that the control probe is a stilt that extends between the oligomer test probe and the surface, such that each feature comprises the control stilt and the oligomer test probe.

38. The method of making of Claim 30, wherein the step of providing the control probe comprises the step of adding one end of the control probe to the surface of the microarray substrate; and the step of providing the oligomer test probe comprises the step of adding one end of the oligomer test probe to the surface of the substrate at each feature location, such that each feature comprises the control probe and the oligomer test probe.

39. The method of making of Claim 30, wherein the step of providing the control probe comprises the steps of:

presynthesizing the control probe; and

attaching one end of the presynthesized control probe to the surface of the substrate within each feature.

40. The method of making of Claim 39, wherein the step of providing the oligomer test probe comprises the step of:

presynthesizing the oligomer test probe; and

attaching the presynthesized oligomer test probe within each feature.

41. The method of making of Claim 40, wherein the step of attaching the presynthesized oligomer test probe comprises attaching the presynthesized oligomer test probe to an opposite end of the presynthesized control probe.

42. The method of making of Claim 39, wherein the step of providing the oligomer test probe comprises the step of:

synthesizing the oligomer test probe *in situ* within each feature.

43. The method of making of Claim 42, wherein the *in situ* synthesized oligomer test probe is synthesized on an opposite end of the presynthesized control probe.

44. The method of making of Claim 30, wherein the step of providing the control probe comprises the step of:

synthesizing the control probe *in situ* on the surface of the substrate within each feature.

45. The method of making of Claim 44, wherein the step of providing the oligomer test probe comprises the step of:

presynthesizing the oligomer test probe; and

attaching the presynthesized oligomer test probe within each feature.

46. The method of making of Claim 45, wherein the step of attaching the presynthesized oligomer test probe comprises attaching the presynthesized test probe to an unattached end of the *in situ* synthesized control probe.

47. The method of making of Claim 44, wherein the step of providing the oligomer test probe comprises the step of:
5 synthesizing the oligomer test probe *in situ* within each feature.

48. The method of making of Claim 47, wherein the *in situ* synthesized oligomer test probe is synthesized on an unattached end of the *in situ* synthesized control probe.

49. The method of making of Claim 30, wherein the steps of providing the control probe and providing the oligomer test probe comprises the steps of:
10 presynthesizing the control probe;
attaching one end of the presynthesized control probe to the surface of the substrate within each feature; and
15 synthesizing the oligomer test probe *in situ* on an opposite end of the presynthesized control probe.

50. A method of detecting hybridized features on a microarray using a microarray scanner comprising the steps of:
providing a microarray having a microarray substrate that comprises:
20 a control probe attached at one end in an array pattern of features on a surface of the substrate; and
an oligomer test probe added to each feature location;
providing a control-specific target material complementary to the control probe, wherein the control target comprises a control target label that emits a control
25 target signal when excited by a light; and
providing the microarray and the labeled control target material to a user to perform a hybridization assay with a test target sample.

51. The method of detecting hybridized features of Claim 50, wherein the control probe is directly associated with a control probe label that emits a control probe signal when excited by the light, the control probe signal being different from the control target signal.

5 52. The method of detecting hybridized features of Claim 51, wherein before the step of providing the microarray to a user, the microarray is interrogated with scanning equipment to excite the control probe label and obtain quality control data based on the control probe signal, and the step of providing the microarray to a user further comprises providing the data to the user.

10 53. The method of detecting hybridized features of Claim 50, wherein the oligomer test probe is directly associated with a test label that emits a test signal when excited by the light, the test signal being different from the control target signal.

15 54. The method of detecting hybridized features of Claim 50, wherein after the step of providing the microarray to a user, further comprising the step of performing a hybridization assay on the microarray with the test target sample, such that the hybridized oligomer test probe is associated with a test label that emits a test signal when excited by the light, the test signal being different from the control target signal.

20 55. The method of detecting hybridized features of Claim 54, wherein after the step of performing the assay, further comprising interrogating the hybridized microarray with the microarray scanner to obtain assay results, the step of interrogating comprising collecting the control target signal detected in a control channel and collecting the test signal detected in a test channel that is separate from the control channel of a detection system of the scanner.

25 56. The method of detecting hybridized features of Claim 55, wherein after the step of interrogating, further comprising the step of transmitting data representing the all or part of the assay results.

57. The method of detecting hybridized features of Claim 56, wherein after the step of transmitting data, further comprising the step of receiving the data.

58. The method of detecting hybridized features of Claim 55, wherein the assay results are analyzed at a first location, the method further comprising
5 communicating the assay results or a conclusion based on the assay results to a second location remote from the first location.

59. The method of detecting hybridized features of Claim 58, wherein the test target sample is obtained from a third location remote from the first location or the second location.

60. A method of locating hybridized features on a microarray using a
10 microarray scanner, the microarray having oligomer test probes in an array pattern of features on a substrate, the oligomer test probes for hybridizing with a target sample under test at one or more features, the hybridized oligomer test probes being labeled with a test label that emits a test signal when excited with a light, the method
15 comprising the steps of:

providing a control probe to a surface of the substrate at each feature location, such that each feature comprises the control probe and the oligomer test probe;

associating a control label with the control probe, the control label emitting a control signal when excited with the light, the control signal being different from the
20 test signal; and

interrogating the microarray substrate with the microarray scanner to locate the hybridized oligomer test probes by detecting the control signals at each feature and separately detecting the test signals from the one or more features and correlating the detected signals.

61. The method of locating hybridized features of Claim 60, wherein the step
25 of associating a control label comprises the step of directly labeling the control probe with a control probe label that emits a control probe signal when excited by the light.

00507075.10300

62. The method of locating hybridized features of Claim 61, wherein the step of associating a control label further comprises the step of providing a control-specific target material complementary to the control probe, wherein the control target comprises a control target label that emits a control target signal when excited by the light, the control target signal being different from the control probe signal, the control target label being indirectly associated with the control probe upon hybridization with the control specific target material.

63. The method of locating hybridized features of Claim 60, wherein the step of associating a control label comprises the step of providing a control-specific target material complementary to the control probe, wherein the control target comprises a control target label that emits a control target signal when excited by the light, the control target signal being different from the control probe signal, the control target label being indirectly associated with the control probe upon hybridization with the control specific target material.

64. The method of locating hybridized features of Claim 63, wherein in the step of providing a control-specific target material, the control-specific target material is hybridized to the control probe at the time the oligomer test probes are hybridized to the test target sample.

65. The method of locating hybridized features of Claim 60, wherein the control probe is provided prior to the oligomer test probes, the oligomer test probes are attached to the control probes at each feature and the control probe acts as a stilt extending the oligomer test probe from the surface of the substrate.

66. The method of locating hybridized features of Claim 60, wherein in the step of interrogating, the microarray scanner has a separate channel for detecting the test signals from the hybridized oligomer test probes and a separate channel for detecting the control signal from the control probe.

67. The method of locating hybridized features of Claim 62, wherein in the step of interrogating, the microarray scanner has a test channel for detecting the test

-58-

signals from the hybridized oligomer test probes, a separate control channel for detecting the control probe signal from the control probe, and another separate control channel for detecting the control target signal from the hybridized control probe.

68. A method of detecting features on a microarray with a microarray scanner, the microarray comprising a substrate having a surface, the method comprising the steps of:

providing a control probe to the substrate in an array pattern of features on the surface of the substrate, the control probe being associated with a control label that emits a control signal when exposed to a light; and

providing an oligomer test probe to each feature location, such that each feature comprises the control probe and the oligomer test probe;

interrogating the microarray with the microarray scanner to detect the control signal; and

evaluating data collected on the detected control signal.

69. The method of detecting features of Claim 68, wherein the oligomer test probe is associated with a test label that emits a test signal when exposed to the light, the test signal being different from the control signal.

70. The method of detecting features of Claim 69, wherein the step of interrogating comprises the steps of:

scanning the microarray substrate with a light to excite the control label and the test label; and

detecting the control signal from each feature in a control detection channel of the scanner; and

separately detecting the test signal in a separate test detection channel of the scanner.

71. The method of detecting features of Claim 68, wherein the control label is associated directly with the control probe.

72. The method of detecting features of Claim 71, wherein the step of interrogating comprises detecting the control signal at each feature location to obtain quality control data on the microarray.

73. The method of detecting features of Claim 69, wherein before the step of interrogating, the method further comprises the step of exposing the microarray to a hybridization solution comprising a target sample under test comprising the test label; and wherein the step of evaluating comprises determining characteristics of the hybridization between the oligomer test probe and the test target sample at each feature location.

74. The method of detecting features of Claim 73, the hybridization solution further comprises a control-specific target material complementary to the control probe, the control target comprising the control label, such that the control label and test label are indirectly associated with the control probe and the oligomer test probe, respectively, by hybridization.

75. The method of detecting features of Claim 74, wherein the step of interrogating comprises the steps of:
detecting the control signal from the hybridized control probe at each feature location;
detecting the test signals from the hybridized oligomer test probes; and
using the detected control signals as reference data to normalize with the detected test signals.

76. The method of detecting features of Claim 74, wherein the control label comprises a control probe label and a control target label, the control probe label being associated directly with the control probe, the control target label being indirectly associated with the control probe by hybridization, and the control target comprising the control target label, and wherein the control probe label emits a control probe signal and the control target label emits a control target signal that is different from the control probe signal, and wherein both the control probe signal and the control target signal are different from the test signal.

77. The method of detecting features of Claim 76, wherein the step of interrogating comprises the steps of:

scanning the microarray substrate with a light to excite the control labels and the test label; and

5 detecting the control probe signal in a control probe detection channel of a control channel of the scanner;

separately detecting the control target signal in a separate control target detection channel of the control channel; and

10 further separately detecting the test signal from the hybridized oligomer test probes in a separate test detection channel of the scanner.

78. The method of detecting features of Claim 76, further comprising the step of first interrogating the microarray with a microarray scanner before the step of exposing the microarray to a hybridization solution, wherein the step of first interrogating comprises detecting the control probe signal at each feature location to
15 obtain quality control data on the microarray, and wherein after the step of exposing, the step of interrogating the hybridized microarray comprises the steps of:

detecting the control target signal from the hybridized control probe at each feature location;

20 detecting the test signals from the hybridized oligomer test probe; and

using the detected control target signals as reference data to normalize with the detected test signals.

79. A kit for evaluating a sample of a test target nucleic acid sequence comprising:

25 an apparatus comprising a microarray substrate, a control probe attached in an array pattern of features on a surface of the substrate, and an oligomer test probe attached at each feature location;

a control-specific target material complementary to the control probe, wherein the control target comprises a control target label that emits a control target signal; and

30 instructions for using the apparatus and control target material.

20250324

81. The kit of Claim 80, wherein the instructions comprise quality data about
5 the apparatus obtained by interrogation of the apparatus with a microarray scanner to
evaluate the control probe signal at each feature location.

83. The kit of Claim 79, wherein the oligomer test probe comprises a test probe label that emits a test probe signal, the test probe signal being different from the control target signal.

Ad d B1

[illegible]